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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/599,152	06/21/2000	David J. Yang	UTXC:664	6919

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EXAMINER
JONES, DAMERON LEVEST

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 04/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/599,152	Applicant(s) YANG ET AL.	
	Examiner D. L. Jones	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-5,9-12,15,16,18,22 and 33-41* is/are rejected.

7)☒ Claim(s) *6-8,13,14,17, 19-21, and 23-32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of Paper No. 9, filed 2/4/02, wherein claims 1 and 42-51 were canceled and claims 2-32 were amended.

Note: Claims 2-41 are pending.

112 REJECTIONS

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 9 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9, line 3: A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74

(Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 9 recites the broad recitation that the marker is a monoclonal antibody, and the claim also recites a specific type, antisense, antibody which is the narrower statement of the range/limitation.

Claim 22: The claim as written is ambiguous because it depends on 'claim 0'. Applicant is respectfully requested to make the appropriate correction.

103 REJECTIONS

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 2-5, 10-12, and 33-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ilgan et al (Cancer Biotherapy & Radiopharmaceuticals, Dec. 1998, Vol. 13, No. 6, pages 427-435).

Ilgan et al disclose Tc-99m-ethylenedicysteine(EC)-folate as a tumor imaging agent (see entire document, especially, abstract). In addition, Ilgan et al disclose (1) the biodistribution of Tc-99m-EC-folate in various organs/tissues/fluids such as blood, lung, liver, stomach, kidney, thyroid, muscle, intestine, urine, and tumor (page 431, Table 2). (2) In Figures 4 and 5, page 433, images of the subject are disclosed.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to synthesize a composition for imaging comprising a radionuclide, ethylenedicysteine, and a tissue specific ligand because the prior art disclose an imaging agent comprising the composition components as set forth by Applicant.

6. Claims 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mangera et al (1999, Journal of Labelled Compounds and Radiopharmaceuticals, Vol. 42, pages 683-699).

Mangera et al disclose the synthesis and evaluation of Tc-99m-ethylene dicysteine (EC) as a possible label for bioactive compounds such as peptides , diphosphonates, and other compounds. However, the reference fails to disclose a specific example wherein a bioactive compound is attached to 99mTc-Ec.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Mangera et al and synthesize a composition for imaging comprising a radionuclide, EC, and a tissue specific ligand because Mangera et al suggests the attachment of a bioactive compound such as a peptide to their Tc-99m-EC conjugate.

7. Claims 2-5, 15, 16, 18, and 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable Zareneyrizi et al (Anti-Cancer Drugs, 1999, Vol. 10, pages 685-692).

Zareneyrizi et al disclose the synthesis of Tc-99m-ethylenedicysteine-colchicine for the evaluation of anti-angiogenic effect (see entire document, especially, abstract).

In addition, Zareneyrizi et al disclose (1) the biodistribution of Tc-99m-EC-colchicine in various tissues/organs such as blood, lung, liver, spleen, kidney, muscle, stomach, uterus, thyroid, and tumor (page 689, Table 1). (2) Images of subjects administered Tc-99m-EC-colchicine are disclosed on page 690, Figure 5.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to synthesize a composition for imaging comprising a radionuclide, ethylenedicysteine, and a tissue specific ligand because the prior art disclose an imaging agent comprising the composition components as set forth by Applicant.

8. Claims 2-5, 15, 16, and 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable Yang et al (Pharmaceutical Research, 1999, Vol. 16, No. 5, pages 743-750).

Yang et al discloses Tc-99m-ethylenedicysteine-metronidazole for assessment of tumor hypoxia (see entire document, especially, abstract). In addition, Yang et al disclose the biodistribution of Tc-99m-EC-metronidazole in various tissues/organs such as blood, lung, liver, spleen, kidney, muscle, intestine, thyroid, and tumor (page 745, Table 1). (2) Images of a subject administered Tc-99m-EC-metronidazole in Figure 4, page 748.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to synthesize a composition for imaging comprising a radionuclide, ethylenedicysteine, and a tissue specific ligand because the prior art disclose an imaging agent comprising the composition components as set forth by Applicant.

9. Claims 2, 3, 33, and 34, are rejected under 35 U.S.C. 103(a) as being unpatentable Anderson et al (Nucl. Med. Biol., 1995, Vol. 22, No. 2, pages 165-173).

Anderson et al disclose Ga and In labeled ethylenedicysteine complexes for in vivo studies (see entire document, especially, abstract). In addition, Anderson et al disclose (1) that as a result of the EC complexes being stable in vivo, the derivatives may have applications as bifunctional chelates for protein and peptides (abstract, page 165, 'Introduction'). 2) On pages 171-172. Tables 5 and 6, the biodistribution of Ga-EC and In-EC in various tissues/organs such as blood, lung, liver, spleen, kidney, muscle, heart, brain, bone, stomach, and small and large intestines is disclosed.
Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to synthesize a composition for imaging comprising a radionuclide, ethylenedicysteine, and a tissue specific ligand because the prior art suggests that the since the EC derivatives are stable in vivo, derivatives of EC may have application as bifunctional chelates for proteins and peptides.

10. Claims 2-5 and 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable Anderson et al (Nucl. Med. Biol., 1995, Col. 22, No. 2, pages 165-173) in view of Marzilli et al (US Patent No. 5,986,074) *or* Bergstein et al (US Patent No. 5,279,811).

Anderson et al (see discussion above) fails to disclose the making of their compositions with technetium-99m.

Bergstein et al disclose ester-substituted diaminodithiols and radiolabeled complexes thereof (see entire document, especially, abstract). In particular,

ethylenedicysteine derivatives are encompassed in formula A of Bergstein et al when two of R1-R12 are A-COOR (A is zero carbon atoms and R is alkyl), o, p, and n are 1, and the other R1-R12 are hydrogen (column 2, lines 34-64; column 4, lines 1-29). (2) the diaminodithiols may be radiolabeled with various radionuclides including Cu, Tc, Fe, and Re (column 3, lines 48-57).

Marzilli et al disclose metal chelates that may be are useful as pharmaceutical imaging agents comprising ethylenedicysteine and derivatives thereof (see entire document, especially, abstract; columns 3-4, lines 45-68 and 1-36, respectively; columns 24-25, Example 4). In addition, Marzilli et al disclose (1) the chelates may be radiolabeled with 99m-Tc (column 4, lines 37-44). (2) The EC complex may be one of the components present in a diagnostic/therapeutic kit (column 10, lines 36-41; columns 19-20, lines 59-68 and 1-34, respectively). (3) Table 1, (column 12), discloses the biodistribution of subjects administered the EC complex.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Anderson et al using the teachings of Bergstein et al and Marzilli et al and synthesize a composition for imaging comprising a radionuclide (technetium-99m), ethylenedicysteine, and a tissue specific ligand because the secondary references disclose that labeling EC with technetium-99m is well known in the art. Since each of the cited references is directed to EC complexes for imaging purposes, the references may be considered to be within the same field of endeavor. Hence, the references are combinable.

CLAIM OBJECTIONS

11. Claims 6-8, 13, 14, 17, and 19-21, and 23-32 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Note: The claims are allowable over the prior art of record because the prior art neither anticipates nor renders obvious the methods having the additional limitations as set forth in the dependent claims (e.g., i.e., Tc-99m-EC-methotrexate; Tc-99m-EC-tomudex, Tc-99m-EC-annexin V, Tc-99m-EC-metronidas, or Tc-99m-EC-glutamate pentapeptide).

SPECIFICATION

12. This application filed under former 37 CFR 1.60 lacks the necessary reference to the prior application. A statement reading "This is a CIP of Application No. 09/434,313, filed 10/25/99, which is a CIP of Application No. 09/587,583, filed 6/2/2000." should be entered following the title of the invention or as the first sentence of the specification. Also, the current status of all nonprovisional parent applications referenced should be included.

COMMENTS/NOTES

13. Applicant is respectfully requested to make of record the declarations submitted in the parent application indicating that the cited references (Ilgan et al, Mangera et al, Zareneyrizi et al, and Yang et al) are not available as prior art on

the basis that none of the non-invention authors of the cited references can be considered inventors of the instant subject matter.

14. Applicant is respectfully requested to replace '(with or without linker)' with 'wherein a linker is optionally present' in claim 35, lines 6-7, for clarity of the claim.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (703) 308-4640. The examiner can normally be reached on Mon.-Fri. (alternate Mon.), 6:45 a.m. - 4:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose' Dees can be reached on (703) 308- 4628. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

D. L. Jones
Primary Examiner
Art Unit 1616

April 19, 2002